REMARKS

Upon entry of this Amendment, claim 9 will be amended; claims 12-14 will be canceled; and claim 15 will be added. Claims 9-11 and 15 are pending and under consideration. Reconsideration and allowance of the application are respectfully requested.

Support for the Amendments can be found throughout the specification and original claims. For example, support for the amendment to claim 9 can be found, *inter alia*, at the second full paragraph on page 12 of the specification. Support for new claim 15 can be found, e.g., at Example 5 on pages 16-20 of the specification, including Table 1 on page 19, as well as Figures 4A-4C. No new matter has been added.

Entry of this amendment is appropriate after final rejection because it seeks to place the application into condition for allowance while reducing issues for appeal. The amendment responds to rejections set forth in the Final Office Action, and even more clearly recites the claimed subject matter.

Response To Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Final Office Action rejects claims 9-14 as allegedly indefinite for failing to define the meaning of "a control value" against which the sample measurement is compared. In particular, the rejection asserts that the ordinary artisan could not determine the meets and bounds for practicing the method claims, at least insofar as it is allegedly unclear whether, e.g., "an ascertained amount of protein, mRNA or cDNA for GPC3," a "control amount of an irrelevant protein, mRNA or cDNA used in a standard curve," or a "normal skin cell or some normal cell type equivalent for malignant melanoma" is intended (see Final Office Action at paragraph bridging pages 3-4).

In response, and without acquiescing to the propriety of the rejection, Applicants submit that the claimed subject matter is now even clearer and more definite. Applicants further submit that one of ordinary skill in the art would immediately know the meaning of a "control value," and that a definition for the term "control value" is not a requisite for definiteness of the claimed subject matter.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested. However, should the Examiner deem that any further amendment would be beneficial to the claims, the Examiner is invited to contact the undersigned to discuss the same.

Response To Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Final Office Action rejects claims 12-14 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the rejection alleges the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In response, and without acquiescing to the propriety of the rejection, Applicants submit that the instant amendment renders the written description rejection of claims 12-14 moot. Accordingly, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph (written description), is respectfully requested.

The Final Office Action also states that the specification provides enabling disclosure for "detecting soluble or membrane associated GPC3 protein using an antibody recognizing an

extracellular domain of the protein (e.g., 303-464) in a method for diagnosing (or at risk of having) malignant melanoma along with other clinically relevant melanoma tumor markers (e.g., 5-S-CD and MIA)" (see Final Office Action at page 5, Section 11). However, the Final Office Action rejects claims 9-11 as allegedly not enabled for practicing a diagnostic method using any anti-GPC3 antibody directed to any epitope on the protein and in the absence of additional art-recognized melanoma biomarkers.

In particular, the Final Office Action asserts that "only antibodies against secreted/soluble GPC3 can be used in the claimed method" and that "the antibodies against GPC3 should be specified and they are not" (Office Action at page 8, first full paragraph). The rejection further asserts that a review of the prior art indicates that "detailed controls including sample control tissues and other art-recognized biomarkers for melanoma having a clinical stage-correlation for melanoma are required to practice the method invention," and that the "ordinary artisan could not have practiced the claimed invention in order to unequivocally diagnose malignant melanoma in any subject using only GPC3 expression as the sole biomarker indicia" (Office Action at page 10, first full paragraph).

In response, Applicants submit that the use of additional art-recognized biomarkers is not required at least because the claims are not directed to the unequivocal diagnosis of malignant melanoma as the Office Action asserts, but rather to methods of determining the likelihood of the presence of melanoma in a subject. Furthermore, the specification makes clear that GPC3 allows for assessment of risk even at very early stages and that other markers, e.g., MIA and 5-S-CD, are reliable at later stages of the disease.

In addition, Applicants submit that the antibodies to GPC3 need not be specified as *any* antibody capable of detecting GPC3 in a sample would appear to be enabled. In support thereof,

Applicants submit that Example 4 and Figure 2, e.g., include detection of membrane-bound GPC3 while Example 5 and Figure 3, e.g., include detection of secreted GPC3.

Applicants also submit that the specification provides guidance with respect to the use of antibodies in the claimed subject matter and that one of ordinary skill in the art would know which antibodies to use depending upon, e.g., the type of sample involved. Applicants further submit that the ordinary level of skill in this art is high, and that one having ordinary skill in the art would be able to make and use the claimed subject matter without undue experimentation based on the guidance provided by Applicants' specification as well as the level of skill of one of ordinary skill in the art. For example, Applicants' specification provides guidance with respect to the detection methods which may be used to measure or detect GPC3 in a sample, including exemplary antibodies/reagents, as well as exemplary procedures for measuring and detecting GPC3 and other tumor markers for melanoma in a sample, etc. (see, e.g., Examples 4-5 on pages 16-20).

In addition, Applicants submit that claimed subject matter is directed, *inter alia*, to methods of determining an increased likelihood of the presence of malignant melanoma in a subject comprising "detecting soluble or membrane-bound GPC3 protein using an antibody recognizing an extracellular domain of the protein along with additional clinically relevant melanoma tumor markers" which subject matter has been identified in the Final Office Action dated January 29, 2010 as enabled (see, e.g., page 5, section 11).

Based on at least the foregoing, Applicants submit that Applicants' specification provides sufficient guidance such that the claimed invention is enabled without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph (enablement) with respect to claims 9-11.

The Final Office Action also states that the specification provides enabling disclosure for "detecting GPC3 mRNA in a solid tissue or cell sample from a melanoma patient" (see Final Office Action at page 10, Section 12). However, the Final Office Action rejects claims 12-14 as allegedly not enabled for diagnosing risk for malignant melanoma based on quantitating the GPC3 mRNA or cDNA, or based on such quantitation in the absence of quantitating another art-recognized melanoma marker that would allow a risk assessment of the subject to melanoma.

In response, and without acquiescing to the propriety of the rejection, Applicants submit that the instant amendment renders the enablement rejection of claims 12-14 moot. Accordingly, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph (enablement), is respectfully requested.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow all the pending claims.

No fee is believed due at this time. If, however, any additional fee is necessary to ensure consideration of the submitted materials, the Patent and Trademark Office is hereby authorized to charge the same to Deposit Account No. 19-0089.

Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully Submitted,
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